

## SCIENCE

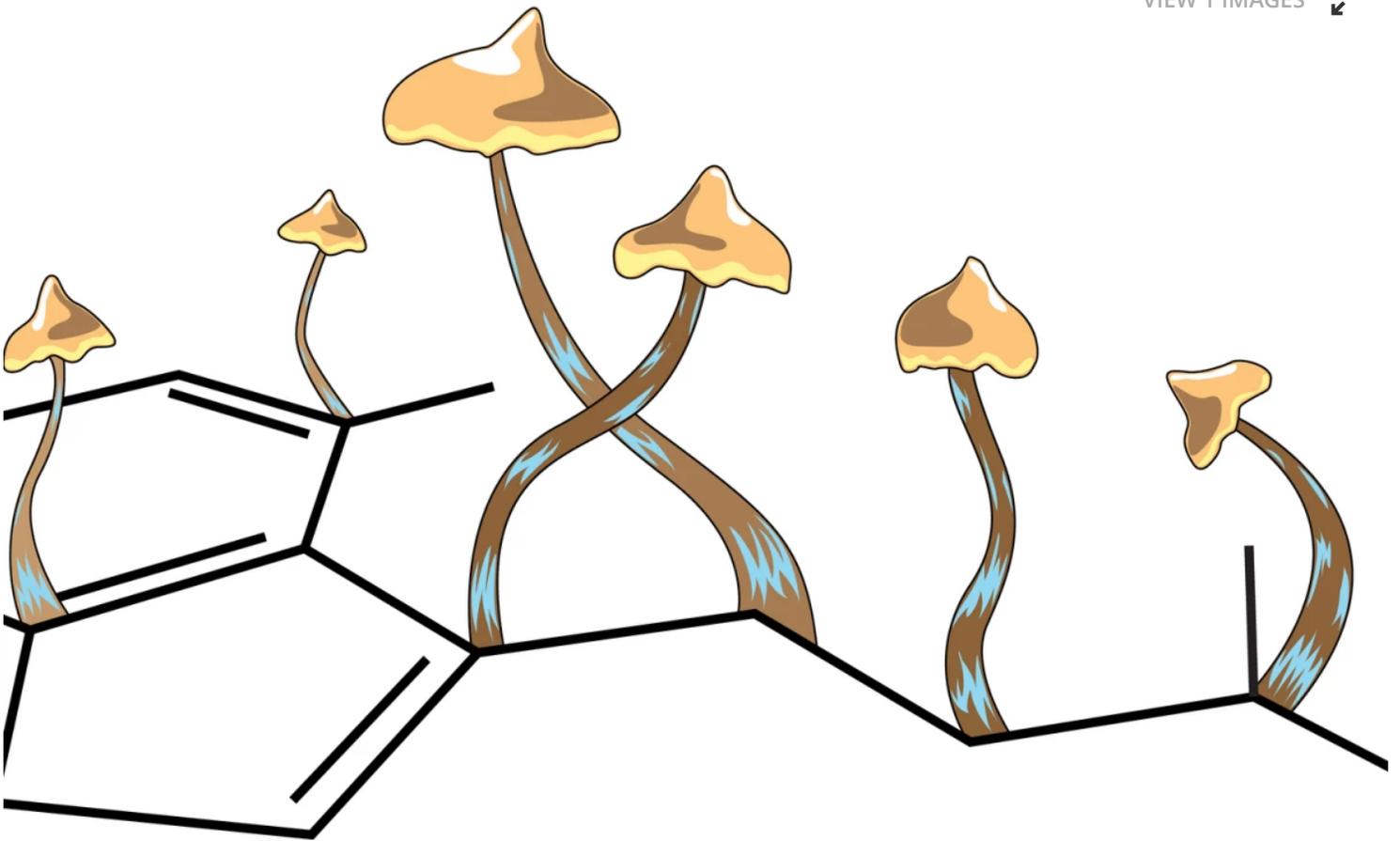
# Landmark study shows one dose of psilocybin induces new neural connections

By Rich Haridy  
July 05, 2021

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*One dose of psilocybin induced rapid growth of dendritic spines in the frontal cortex of mice* [Vox19/Depositphotos](#)

An extraordinary new study from a team of scientists at Yale University is reporting the first direct cellular demonstration of a single psilocybin dose inducing neural plasticity in a mammalian brain. The researchers show how the psychedelic prompts rapid growth of neural

connections in the frontal cortex of mice and hypothesize this mechanism playing a role in the drug's antidepressant qualities.

Over the last decade [psychedelic science](#) has been accelerating at a rate not seen in half a century. [MDMA for PTSD](#) and [psilocybin for depression](#) are both in late-stage human trials and on the verge of clinical approval, however, we still know very little about how these psychedelic compounds actually generate their therapeutic effects.

Years of good study into depression have given psychedelic researchers clues to where they should be looking. We know depression is associated with [synaptic atrophy in the frontal cortex](#). We also know rapid-acting anti-depressants can improve mood by reversing these synaptic deficits, essentially increasing the volume of neuronal connections in these key brain regions.

So, do psychedelics promote that same kind of neural plasticity?

This new research, published in the journal *Neuron*, suggests the answer is yes ... at least in mice.

Using chronic two-photon microscopy the researchers imaged the synaptic architecture of the medial frontal cortex in a number of mice. The imaging focused on the number and density of neuronal connections, called dendritic spines. Seven imaging sessions were conducted, beginning before a single dose of psilocybin was administered and stretching up to a month after.

Within 24 hours of that single psychedelic dose the researchers detected increases in dendritic spine size and density. These changes were noted as occurring extremely quickly and also unexpectedly enduring.

One month later a small amount of these new neuronal connections were still present. Alex Kwan, senior author on the study, says it was surprising to see just one dose of psilocybin lead to persistent structural change in the mice brains.

"We not only saw a 10 percent increase in the number of neuronal connections, but also they were on average about 10 percent larger, so the connections were stronger as well," says Kwan. "It was a real surprise to see such enduring changes from just one dose of psilocybin. These new connections may be the structural changes the brain uses to store new experiences."

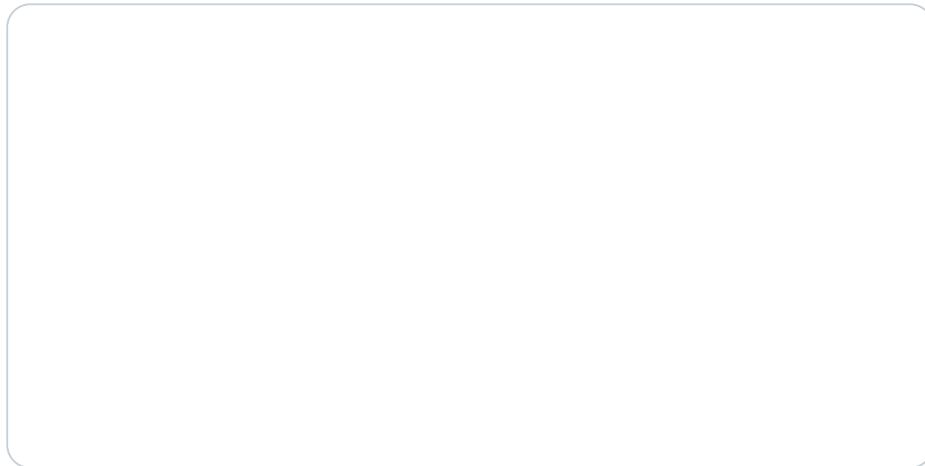


**Alex Kwan 關進晞** @kwanalexc · Feb 17, 2021



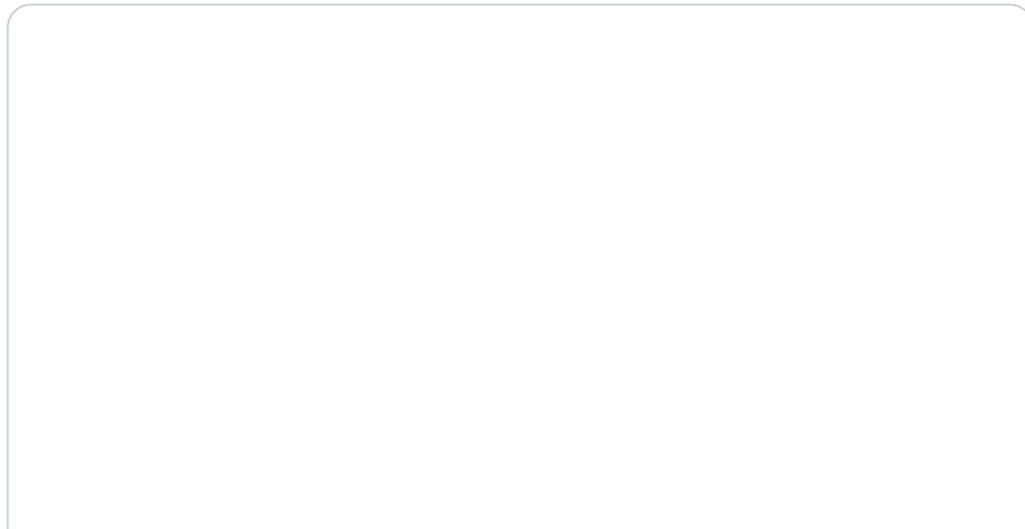
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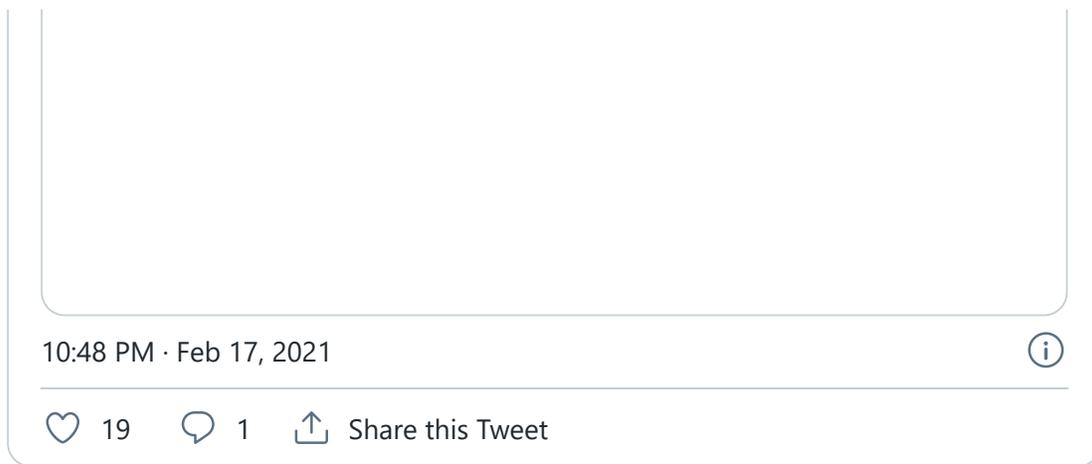
Focusing on 1 mg/kg, we used chronic two-photon imaging to track apical dendritic spines of layer 5 pyramidal neurons in the medial frontal cortex.  
4/7



**Alex Kwan 關進晞**  
@kwanalexc

Administering psilocybin caused ~10% increases in spine density and spine head width, effects that were observed within 1 day of injection. Some of the newly formed spines persisted 1 month later. 5/7





Alongside these structural changes the researchers note functional and behavioral changes were also detected in the animals following the single psilocybin dose. Increased excitatory neurotransmission in the frontal cortex was measured in the mice and stress-related behaviors reduced. This finding suggests these structural brain changes could play a role in some of the therapeutic benefits seen with psychedelics.

Perhaps most interesting is the study's attempt to disassociate the structural brain changes caused by psilocybin from the drug's acute psychedelic effects. The researchers used a drug called ketanserin to block 5-HT<sub>2</sub> receptors, the pathway by which many believe psychedelic drugs induce their acute "trippy" effects.

Ketanserin effectively stifled head-twitch responses in the animals, which is the primary observational measurement used to track acute psychedelic sensations in mice. But the ketanserin did not block any of the psilocybin-induced brain plasticity changes.

"The possibility to disrupt psilocybin's acute behavioral effects without abolishing structural plasticity actions has clear implications for treatment in the clinic," the researchers hypothesize in the study. "However, it is not yet clear if the results will extrapolate to humans."

Whether the therapeutic actions of psychedelics can be separated from the acute effects is perhaps one of the biggest unanswered questions in psychedelic science. The researchers do note ketanserin is known to only block around 30 percent of 5-HT<sub>2</sub> receptors in rodents so it is certainly possible the neural plasticity induced by psilocybin is still mediated through that pathway. A lot more work will be necessary to understand exactly what is going on here, and

the jury is certainly still out on whether these psychedelic drugs can generate therapeutic effects without generating an acute psychedelic experience.

The research is the first to directly demonstrate these specific structural neural changes induced by psilocybin in a mammal brain. Another very recent study looking at the effects of a [single psilocybin dose in a pig brain](#) saw similar signs of psychedelic-induced neural plasticity. That research saw psilocybin increase levels of a key protein known to enhance neuroplasticity.

The new study was published in the journal *Neuron*.

Source: [Yale University](#)

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9 COMMENTS



## Rich Haridy

With interests in film, new media, and the new wave of psychedelic science, Rich has written for a number of online and print publications over the last decade and was Chair of the Australian Film Critics Association from 2013-2015. Since joining New Atlas Rich's interests have broadened to encompass the era-defining effects of new technology on culture and life in the 21st century.

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**czechster** JULY 5, 2021 09:20 PM

Now how do you get past the barbarians in Congress?

**guzmanchinky** JULY 6, 2021 07:22 AM

Well, my wife and I are signed up for a psilocybin session in the Netherlands in September, we shall see how it goes!

**jerryd** JULY 6, 2021 09:26 AM

How come they want to take any fun drug and take the fun out of it? It's doubtful people will have a bad effect from this as so mild not at all like LSD, etc. It's a very pleasant body and color high with interesting visual effects. None of the driving out of control stuff of most others. And alone can make one feel better before new neurons can form.. Just ramp up from low doses would weed out any that can't handle it and make it more enjoyable.

I wish I had some of those we found decades ago to start reproducing them for my own use. If you get a fresh one just open the gills and shake it into mushroom growth media.

Just like pot they want to get rid of the enjoyable parts.

**akarp** JULY 6, 2021 09:54 AM

"we still know very little about how these psychedelic compounds actually generate their therapeutic effects" This is true with just about ALL compounds and therapies...shouldn't stop us from using them for the beneficial effects.

As to Congress...almost all politicians are in it for the money or some other personal gain. Get 'past' them by living your life, do research, take responsibility for your body and what you choose to consume. I don't take a medication just because the FDA says its 'safe', I also don't stop taking a substance just because the FDA says something is 'unsafe.'

**paleochocolate** JULY 6, 2021 10:07 AM

I too would rate it a perfect 5/7.

**Don Duncan** JULY 6, 2021 11:02 AM

Without the FDA, AMA and invasive, unconstitutional drug laws we could have a lot more knowledge to back up the anecdotal reports, and benefit from herbal medicines. But herbs

can't be patented, don't need expensive appointments/prescriptions. Govt. is the biggest racket ever conceived.

**HoppyHopkins** JULY 6, 2021 09:17 PM

Take two mushroom burgers and call me in the morning once you stop tasting the color blue

**Worzel** JULY 7, 2021 04:44 AM

Could it be that the real reason psilocybin was banned, was to stop the hoi polloi becoming too intelligent from its use?

**wolf0579** JULY 7, 2021 08:34 AM

This study bolsters the untestable hypothesis that our ancestors gained consciousness/intelligence by eating the mushrooms growing on the droppings of the animals they were hunting. A few million magic mushroom trips over the millennia and the neurons just keep coming!

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